

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P697PC00	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/DK 03/00901	International filing date (day/month/year) 18/12/2003	(Earliest) Priority Date (day/month/year) 20/12/2002
Applicant ENKAM PHARMACEUTICALS A/S		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 9 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☒ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 03/00901

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-24
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 1-3, 14-25, 29-44 and 54
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

As a result of the prior review under R. 40.2(e) PCT,
no additional fees are to be refunded.

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☒ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-44 and 48-54 (all partly)

directed to a method of modulating the interaction between a fibroblast growth factor receptor and a protein having a binding site comprising SEQ ID NO:1 (NCAM Fn III, FGFR binding motif) and a method of finding compounds which interact with FGFR and a polypeptide comprising the sequence SEQ ID NO: 1.

Invention 2: 1-54 (all partly)

directed to a method of modulating the interaction between a fibroblast growth factor receptor and a protein having a binding site comprising SEQ ID NO2 (Interleukin-6 receptor beta chain, FGFR binding motif) and a method of finding compounds which interact with FGFR and a polypeptide comprising the sequence SEQ ID NO: 2.

Inventions 3-146: claims 1-54,
all partially and as far as applicable.

Subject-matter essentially as defined above for invention 2, but limited to the respective SEQ.ID's 3-146, whereby invention 3 relates to SEQ ID NO:2, invention 3 to SEQ ID NO:3, etc and invention 146 relates to SEQ ID NO:146.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 1-24

Although claims 1- 24 are directed to a method of treatment of the human/animal body, to the extent that they pertain to in vivo use, a search has been carried out, based on the alleged effects of the compound for the parts of the claims which belong to invention 1 and which appear to be clear, supported and disclosed.

Continuation of Box I.2

Claims Nos.: 1-3, 14-25, 29-44 and 54

Present claims 1-3, 14-25, 29-44 and 54 relate to methods using a compound defined by reference to a desirable characteristic or property, namely using a compound being a functional cell-surface receptor, or using a compound comprising at least two immunoglobulin (Ig)-like domains and/or at least two fibronectin type 3 (F3) domains or at least one Ig-like and one F3 domain . Claim 22 refer to a method using a compound being a functional cell-surface receptor and another protein being characterized by having a binding site consisting of one or more "strand-loop-strand" structural motifs. Claims 1, 45 and claims dependent of these claims lack clarity because of the expression "fragments, variants or homologues thereof". The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear; supported and disclosed, namely those parts relating to the method using fibroblast growth factor receptors and a polypeptide having a FGFR binding site comprising SEQ ID NO 1 have been searched.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International Application No.

DK 03/00901

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/566 C07K7/00 //A61K38/00,C07K14/71

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, BIOSIS, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 03 016351 A (SKLADCHIKOVA GALINA ;BOCK ELISABETH (DK); BEREZIN VLADIMIR (DK); E) 27 February 2003 (2003-02-27) See SEQ ID NO:1	1-44, 48-54
X	WO 97 38708 A (GEN HOSPITAL CORP ;SONG HEEKYUNG (US); WANG YUYING (US); GOETINCK) 23 October 1997 (1997-10-23) page 4, line 21 -page 5, line 29; claim 24 -/--	1-44, 48-54

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

21 June 2004

Date of mailing of the international search report

21.12.2004

Name and mailing address of the ISA

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Authorized officer

YVONNE SIÖSTEEN / ELY

INTERNATIONAL SEARCH REPORT

International Application No

/DK 03/00901

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GALINA SKLADCHIKOVA ET AL: "Extracellular adenosine triphosphate affects neural cell adhesion molecule (NCAM-mediated cell adhesion and neurite outgrowth" JOURNAL OF NEUROSCIENCE RESEARCH, vol. 57, 1999, pages 207-218, XP002284206 page 215, right column, line 1 - line 40 and especially line 17 (AENQQGUS), abstract ---	1-44, 48-54
A	WO 91 00916 A (UNIV CALIFORNIA) 24 January 1991 (1991-01-24) page 5, line 16 - line 25 page 25, line 9 ---	1-44, 48-54
A	WO 01 96364 A (IMP COLLEGE INNOVATIONS ;KING S COLLEGE LONDON (GB); SAFFELL JANE) 20 December 2001 (2001-12-20) the whole document ---	1-44, 48-54
A	US 6 255 454 B1 (BARR PHILIP J ET AL) 3 July 2001 (2001-07-03) column 3, line 8 - line 30 ---	1-44, 48-54
A	LARS C. B. RONN ET AL: "Neurite outgrowth induced by a synthetic peptide ligand of neural cell adhesion molecule requires fibroblast growth factor receptor activation" JOURNAL OF NEUROCHEMISTRY, vol. 75, 2000, pages 665-671, XP002284207 the whole document ---	1-44, 48-54
A	PHILIPP NIETHAMMER ET AL: "Cosignaling of NCAM via lipid rafts and the FGF receptor is required for neuritogenesis" THE JOURNAL OF CELL BIOLOGY, vol. 157, no. 3, 29 April 2002 (2002-04-29), pages 521-532, XP002284208 ISSN: 0021-9525 the whole document ---	1-44, 48-54
A	WO 00 11204 A (LANAHAN ANTHONY A ;BENEKEN JUTTA (US); TU JIAN CHENG (US); WORLEY) 2 March 2000 (2000-03-02) the whole document ---	1-44, 48-54

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INTERNATIONAL SEARCH REPORT

International Application No.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FERDYNAND J KOS ET AL: "Costimulation of T cell receptor-triggered IL-2 production by Jurkat T cells via fibroblast growth factor receptor 1 upon its engagement by CD56" IMMUNOLOGY AND CELL BIOLOGY, vol. 80, 2002, pages 364-369, XP002284209 the whole document ---	1-44, 48-54
A	DATABASE EBI [Online] 1 November 1996 (1996-11-01) retrieved from EMBL Database accession no. Q61945 XP002297229 93% identity in 14aa/49aa with SEQ ID NO 9 & SANTONI, M.J. ET AL: "Differential exon usage involving an unusual slicing mechanism generates at NCAM cDNA in mous brain" EMBO J., vol. 8, 1989, pages 385-392, -----	1-44, 48-54

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/DK 03/00901

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03016351	A	27-02-2003	CA 2457164 A1	27-02-2003
			WO 03016351 A2	27-02-2003
			EP 1434798 A2	07-07-2004
WO 9738708	A	23-10-1997	EP 0991422 A1	12-04-2000
			JP 2001519765 T	23-10-2001
			WO 9738708 A1	23-10-1997
WO 9100916	A	24-01-1991	AT 179862 T	15-05-1999
			AU 638734 B2	08-07-1993
			AU 6077990 A	06-02-1991
			CA 2063431 A1	07-01-1991
			DE 69033109 D1	17-06-1999
			DE 69033109 T2	18-11-1999
			DK 481000 T3	15-11-1999
			EP 0481000 A1	22-04-1992
			ES 2133271 T3	16-09-1999
			HU 61052 A2	30-11-1992
			JP 4506604 T	19-11-1992
			KR 235266 B1	15-12-1999
			NO 920060 A	02-03-1992
			SG 72657 A1	23-05-2000
			WO 9100916 A2	24-01-1991
			US 5707632 A	13-01-1998
			US 6355440 B1	12-03-2002
			US 6350593 B1	26-02-2002
			US 6384191 B1	07-05-2002
WO 0196364	A	20-12-2001	EP 1294744 A2	26-03-2003
			WO 0196364 A2	20-12-2001
			US 2004102370 A1	27-05-2004
US 6255454	B1	03-07-2001	US 5229501 A	20-07-1993
WO 0011204	A	02-03-2000	AU 772105 B2	08-04-2004
			AU 5779899 A	14-03-2000
			EP 1105734 A2	13-06-2001
			JP 2002523056 T	30-07-2002
			WO 0011204 A2	02-03-2000
			US 2003170807 A1	11-09-2003
			US 6720175 B1	13-04-2004

Box No. VIII (iv) DECLARATION: INVENTORSHIP (only for the purposes of the designation of the United States of America)
The declaration must conform to the following standardized wording provided for in Section 214; see Notes to Boxes Nos. VIII, VIII (i) to (v) (in general) and the specific Notes to Box No. VIII (iv). If this Box is not used, this sheet should not be included in the request.

**Declaration of inventorship (Rules 4.17(iv) and 51bis.1(a)(iv))
 for the purposes of the designation of the United States of America:**

I hereby declare that I believe I am the original, first and sole (if only one inventor is listed below) or joint (if more than one inventor is listed below) inventor of the subject matter which is claimed and for which a patent is sought.

This declaration is directed to the international application of which it forms a part (if filing declaration with application).

This declaration is directed to international application No. PCT/ DK03/00901 (if furnishing declaration pursuant to Rule 26ter).

I hereby declare that my residence, mailing address, and citizenship are as stated next to my name.

I hereby state that I have reviewed and understand the contents of the above-identified international application, including the claims of said application. I have identified in the request of said application, in compliance with PCT Rule 4.10, any claim to foreign priority, and I have identified below, under the heading "Prior Applications," by application number, country or Member of the World Trade Organization, day, month and year of filing, any application for a patent or inventor's certificate filed in a country other than the United States of America, including any PCT international application designating at least one country other than the United States of America, having a filing date before that of the application on which foreign priority is claimed.

Prior Applications: Danish application No.: PA. 2002 01982, filed 20. December 2002 and danish application No.: PA 2003 00330, filed 3 March 2003.

I hereby acknowledge the duty to disclose information that is known by me to be material to patentability as defined by 37 C.F.R. § 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the PCT international filing date of the continuation-in-part application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name: **BEREZIN, Vladimir**

Residence: **Copenhagen, Denmark**

(city and either US state, if applicable, or country)

Mailing Address: **Nørrebrogade 223, 1.th., 2200 Copenhagen N.**

Citizenship: **Ukrainian**

Inventor's Signature: *Vladimir Berezin*
 (if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: *16.07.2004*
 (of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)

Name: **BOCK, Elisabeth**

Residence: **Charlottenlund, Denmark**

(city and either US state, if applicable, or country)

Mailing Address: **Tonysvej 20, 2920 Charlottenlund**

Citizenship: **Danish**

Inventor's Signature: *Elisabeth Bock*
 (if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: *16 January 2004*
 (of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)

☒ This declaration is continued on the following sheet, "Continuation of Box No. VIII (iv)".

Continuation of Box No. VIII (i) (v) **DECLARATION**

If the space is insufficient in any of Boxes Nos. VIII (i) to (v) to furnish all the information, including in the case where more than two inventors are to be named in Box No. VIII (iv), in such case, write "Continuation of Box No. VIII..." (indicate the item number of the Box) and furnish the information in the same manner as required for the purposes of the Box in which the space was insufficient. If additional space is needed in respect of two or more declarations, a separate continuation box must be used for each such declaration. If this Box is not used, this sheet should not be included in the request.

Continuation of Box No. VIII (iv)

Name: ALBRECHTSEN, Morten

Residence: Charlottenlund, Copenhagen

Mailing address: Høstvej 7, 2920 Charlottenlund

Citizenship: Danish

Inventor's signature: 

Date: 16/11-2004